WEST

End of Result Set

Generate Collection | Print

L1: Entry 1 of 1 File: USPT Aug 5, 2003

US-PAT-NO: 6602709
DOCUMENT-IDENTIFIER: US 6602709 B1

TITLE: Methods for use of apoptotic cells to deliver antigen to dendritic cells for induction or tolerization of T cells

DATE-ISSUED: August 5, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Albert; Matthew L.	New York	NY		
Bhardwaj; Nina	West Orange	NJ		
Steinman; Ralph M.	Westport	CT		
Inaba; Kayo	Kyoto			JP
Darnell; Robert	Pelham	NY		

US-CL-CURRENT: 435/372; 424/184.1, 424/277.1, 424/278.1, 435/2, 435/366, 435/372.1, 435/373

CLAIMS:

We claim:

1. A method of delivering antigen to dendritic cells in vitro, said method comprising: contacting dendritic cells capable of internalizing antigens for presentation to immune cells with apoptotic cells comprising said antigen to be presented to immune cells wherein said contact is for a time sufficient to allow said antigen to be internalized by the dendritic cells.

2. The method according to claim 1 wherein the dendritic cells are human.

3. The method according to claim 1 wherein the apoptotic cells are selected from the group consisting of cells of a cell line, cells which have been transformed to express a foreign antigen, tumor cell line, xenogeneic cells, or tumor cells.

4. The method according to claim 3 wherein the apoptotic cells are selected from the group consisting of monocytes, 293 cells, L cells, Hela cells, B cells and EL4 cells.

5. The method according to claim 1 further comprising the step of inducing apoptosis of cells expressing said antigen to produce the apoptotic cells.

6. The method according to claim 5 wherein apoptosis is induced by infection with influenza virus.

7. The method according to claim 5 wherein apoptosis is induced by irradiation with ultraviolet light, gamma radiation, steroids, serum deprivation, cytokines, or drugs which induce apoptosis.

8. The method according to claim 5 wherein said apoptotic cells are induced to become apoptotic in vitro.

9. The method according to claim 8 wherein apoptosis is induced in vitro by depriving cells comprising said antigen of nutrients in the cell culture medium.

10. The method according to claim 1 wherein dendritic cells are exposed to a preparation of apoptotic cell fragments, blebs, or bodies containing antigen.

11. The method according to claim 1 wherein said antigen is selected from a group consisting of tumor antigens, viral antigens, pathogens, microbial antigens, self antigens, and autoimmune antigens.

12. The method according to claim 11 wherein the antigen is selected from the group consisting of influenza virus, malaria, HIV, EBV, human papilloma virus, CMV, renal cell carcinoma antigens, melanoma antigens, breast cancer antigens, cancer antigens and myeloma antigens.

13. The method according to claim 11 wherein the antigen is a tumor antigen.

14. The method according to claim 1 wherein said dendritic cells are immature and phagocytic.

15. The method according to claim 1 wherein the cells to be induced to undergo apoptosis are first transformed with DNA encoding said antigen.

16. The method according to claim 1 wherein the ratio of apoptotic cells to dendritic cells is about 1-10 apoptotic cells to about 100 dendritic cells.

17. The method according to claim 1 further comprising a maturation step following internalization of said apoptotic cells by said dendritic cells wherein said dendritic cells are exposed to a maturation factor for a sufficient time to induce maturation of said dendritic cells.

18. The method according to claim 17 wherein the maturation step comprises contacting CD83 negative dendritic cells with at least one maturation factor selected from the group consisting of monocyte conditioned medium that causes CD83 negative dendritic cells to mature so as to express CD83, TNF.alpha., IL-1.beta., IL-6, PGE.sub.2, IFN.alpha., CD40 ligand, and necrotic cells.

19. The method according to claim 18 wherein the maturation factor is selected from the group consisting of monocyte conditioned medium; IFN.alpha. and at least one other factor selected from the group consisting of IL-1.beta., IL-6 and TNF.alpha.; and necrotic cells.

20. The method according to claim 19 wherein the maturation factor is necrotic cells.

21. The method according to claim 1 wherein the antigen is produced recombinantly.

22. The method according to claim 21 wherein said apoptotic cells comprise said recombinantly produced antigen prior to becoming apoptotic.

23. The method according to claim 1 wherein the antigen is a tumor antigen of cellular or viral origin.

24. The method of claim 1 wherein said dendritic cells are CD83 negative dendritic cells and maintaining the CD83 negative cells CD83 negative during said contacting.

25. The method of claim 1 wherein the antigen is of viral origin.

26. The method of claim 1 wherein the antigen is an autoantigen.